

CLAIMS

- 5 1. Diagnostic agent comprising a compound of formula :
(PEPTIDE)_{n1} – (LINKER)_{n2} – (SIGNAL)_{n3} (I)
wherein
1) PEPTIDE is chosen in the group :
a) X1 – X2 – X3 – X4 – NHOH (II),
10 wherein
X1 is absent or X1 is a residue of an alpha-amino glycine, X2 is a residue
of an amino acid selected from proline, hydroxyproline, thioproline and
alanine, X3 is a residue of an amino acid selected from glutamine, glutamic
acid, leucine, isoleucine and phenylalanine and X4 is a residue of an alpha-
15 amino acid selected from glycine, alanine, valine, leucine ;
and the hydrogen atom of the amino group in said alpha-amino acid X1
may be replaced with a member X0 selected from the group consisting of
acetyl, benzoyl (Bz), benzyloxy, t-butyloxycarbonyl, benzyloxycarbonyl (Z),
p-aminobenzoyl (ABz), p-amino-benzyl, p-hydroxybenzoyl (HBz), 3-p-
20 hydroxyphenylpropionyl (HPP).

b) a peptide functionally equivalent to a peptide of a)
c) a peptidic fragment of (II) functionally equivalent to a peptide of a) or b)

25 2) SIGNAL is a signal entity for medical imaging
3) LINKER eventually absent represents a chemical link between PEPTIDE
and SIGNAL
; and the pharmaceutical salts thereof.
- 30 2. Diagnostic agent of claim 1 wherein X1 is absent or X1 is glycine, X2 is
a residue of an amino acid selected from proline, hydroxyproline,

thioproline, X3 is a residue of an amino acid selected from leucine, isoleucine and phenylalanine and X4 is a residue of an alpha-amino acid selected from glycine, alanine.

- 5 3. Diagnostic agent of claim 1 wherein PEPTIDE is X-NHOH with X chosen among : Abz-Gly-Pro-D-Leu-D-Ala, HBz-Gly-Pro-D-Leu-D-Ala, Abz-Gly-Pro-Leu-Ala, Bz-Gly-Pro-D-Leu-D-Ala, Bz-Gly-Pro-Leu-Ala, HPP-Pro-D-Leu-D-Ala, HPP-Pro-Leu-Ala, Z-Pro-D-Leu-D-Ala, Z-Pro-Leu-Ala.
4. Diagnostic agent of claim 1 to 3 wherein PEPTIDE is p-aminobenzoyl-
10 Gly-Pro-D-Leu-D-Ala-NHOH.
5. Diagnostic agent of claim 1 to 4 wherein SIGNAL is macrocyclic or linear chelate chosen among DTPA, DOTA, DTPA BMA, BOPTA, DO3A, HPDO3A, TETA, TRITA, HETA, M4DOTA, DOTMA, MCTA, PCTA and the derivatives thereof.
- 15 6. Diagnostic agent of claim 1 to 4 wherein SIGNAL is a lipidic nanoparticule, a liposome, a nanocapsule wherein the SIGNAL is a carrier of a diagnostic metal chelate.
7. Diagnostic agent of claim 1 to 6 wherein said agent is coupled to a metal element M chosen among an ion of a paramagnetic metal of atomic
20 number 21-29, 42-44, or 58-70, namely Gd, or a radionuclide, typically ^{99}Tc , ^{117}Sn , ^{111}In , ^{97}Ru , ^{67}Ga , ^{68}Ga , ^{89}Zr , ^{177}Lu , ^{47}Sc , ^{105}Rh , ^{188}Re , ^{60}Cu , ^{62}Cu , ^{64}Cu , ^{67}Cu , ^{90}Y , ^{159}Gd , ^{149}Pr , ^{166}Ho .
8. Diagnostic agent of claim 1 to 4 wherein SIGNAL is an iron oxide particle.
- 25 9. Diagnostic agent of claim 8 wherein the particle is coated with a gem-bisphosphonate.
10. Use of a compound of claim 9 for the diagnostic of a cardiovascular/atheroma disease.
11. Use of compound of claim 1 to 9 for the preparation of an agent for the
30 diagnostic of a cardiovascular/atheroma disease.

12. Method of preparation of a compound of claim 1 to 8 comprising the coupling of a peptide X1 -X2 -X3 -X4-NHOH and a SIGNAL entity.

13 Method of detecting, imaging or monitoring the presence of matrix metalloproteinase in a patient comprising the steps of: a) administering to
5 said patient a diagnostic agent of claim 1 to 9 ; and b) acquiring an image of a site of concentration of said diagnostic agent in the patient by a diagnostic imaging technique.

10 14 Method of detecting, imaging or monitoring a pathological disorder associated with matrix metalloproteinase activity in a patient comprising the steps of: a) administering to said patient a diagnostic agent according to claim 1 to 9 ; and c) acquiring an image of a site of concentration of said diagnostic agent in the patient by a diagnostic imaging technique.

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15. Method according to claim 14, wherein the atherosclerosis is coronary atherosclerosis or cerebrovascular atherosclerosis.

16. Method of identifying a patient at high risk for transient cerebral
20 ischemic attacks or stroke by determining the degree of active atherosclerosis in a patient comprising carrying out the method of claim 15.

17 Method of identifying a patient at high risk for acute cardiac ischemia, myocardial infarction or cardiac death by determining the degree of active
25 atherosclerosis by imaging the patient by the method of claim 15.